

REMARKS

Please reconsider the application in view of the following remarks. Applicant thanks the Examiner for carefully considering this application.

Disposition of the Claims

Claims 1, 5-7, and 22-25 are pending. Claim 1 is independent. The remaining claims depend, directly or indirectly, from claim 1.

Claim Amendments

Claim 1 has been amended to clarify the invention recited. Support for this amendment can be found, for example, in Reference Example 3 (paragraph [0141]¹ in the published application No. 2005/0222382). Claims 5-7 and 22-25 have been amended to correct formality issues. No new matter is introduced by these amendments.

Rejections under 35 U.S.C. § 103(a)**Claims 1, 5-7, and 22-25**

Claims 1, 5-7, and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meinojohanns (J. Chem. Soc. Perkin Trans. 1, 1998, pages 549-560, PTO-1449 submitted December 20, 2007) (hereinafter “Meinojohanns”) in view of Komba (Journal of Peptide Science, 6: 585-593 (2001), PTO-1449 submitted December 20, 2007) (hereinafter “Komba”) and Ratcliffe (US 5,527,901) (hereinafter “Ratcliffe”). Claim 1 has been amended.

¹ All paragraph numbers referred to are based on the published application No. 2005/0222382.

To the extent that this rejection may still apply to the amended claims, this rejection is respectfully traversed.

Embodiments of the invention relate to a process for preparing a glycopeptide having at least one asparagine-linked oligosaccharide at a desired position of the peptide chain thereof.

Specifically, claim 1 includes, *inter alia*: “preparing an asparagine-linked disialooligosaccharide or an asparagine-linked monosialooligosaccharide having amino group nitrogen protected with a fat-soluble protective group and the carboxyl group of the sialic acid protected with a benzyl, allyl, or diphenylmethyl group, wherein the benzyl, allyl, or diphenylmethyl group is introduced into the carboxyl group of the sialic acid under pH 5 to 6.”

Inventors of the present invention found that the sialic acid carboxyl group can be selectively protected with a benzyl, allyl, or diphenylmethyl group under a specific condition, i.e., pH 5 to 6. Under this condition, the carboxyl group on the asparagine amino acid is not protected by these groups. None of the prior art references teach or suggest this.

Furthermore, as noted in paragraph [0012] of the specification, sialic acid is not stable to the acidic conditions used in solid phase peptide synthesis. Accordingly, there is almost no case wherein oligosaccharides having sialic acid are used for solid-phase synthesis. To solve this problem, a prior art method uses sialyl transferase to transfer an oligosaccharide onto a pre-made oligopeptide, such as the method taught by Meinojohanns cited by the Examiner.

The Examiner acknowledges that Meinojohanns does not teach the use of asparagine-linked oligosaccharide containing protected sialic acid in solid phase synthesis. The Examiner relies on Komba for the teaching of oligosaccharides containing sialic acid that is protected as a methyl ester.

First, Komba teaches an O-linked glycoside, not an N-linked glycoside. Secondly, Komba teaches a solution synthesis, not solid-phase synthesis. Finally, methyl ester is chemically very different from benzyl, allyl, or diphenylmethyl ester protecting group. One skilled in the art would appreciate that methyl esters can be readily prepared with diazomethane. However, there is no diazo equivalent for benzyl, allyl, or diphenylmethyl compounds. Furthermore, methyl ester is difficult to deblock, as recognized by Ratcliffe cited by the Examiner (Col. 2, line 55 – Col. 3, line 5).

The Examiner relies on Ratcliffe for the teaching of benzyl or phenacyl ester of sialic acid. However, these benzyl protected sialic acids are on carbohydrates alone; they are not asparagine-linked. Asparagine also has a carboxylic acid. Ratcliffe does not teach how to protect a sialic acid with a benzyl group when the carbohydrate is linked to asparagine, nor does Ratcliffe teach how to attach the benzyl protected sialyl saccharides to an asparagine amino acid.

The present specification teaches selective protection of a sialic acid carboxyl group in the presence of a competing carboxyl group of the asparagine amino acid. The selective protection makes use of the pKa differential of the two carboxyl groups. The inventors have found that under pH 5 to 6, the carboxyl group of the sialic acid is selected protected, whereas

the carboxyl group on asparagine is not protected. Once the sialic acid is protected with a benzyl, allyl, or diphenylmethyl group, the asparagine-linked saccharide unit can be used on solid-phase synthesis, as recited in the amended claim 1.

Applicant respectfully submits that none of these references provide teaching or suggestion for a combination asserted by the Examiner. The fact that the Examiner is relying on several references for teaching various limitations of the present claim, when none of these reference suggest that they can be combined in a way as disclosed in the present invention, clearly suggests that the Examiner has committed impermissible hindsight reconstruction, using the teaching of the present invention as a road map.

Furthermore, even if these references can be properly combined as asserted by the Examiner, they do not teach or suggest all limitations of the amended claims. As noted above, Ratcliffe does not teach or suggest asparagine-linked saccharide containing a sialic acid protected by a benzyl, allyl, or diphenylmethyl group. Furthermore, both Ratcliffe and Komba teach solution synthesis, not solid-phase synthesis. Meinojohanns teaches conventional solid-phase peptide synthesis, followed by enzymatic grafting of an oligosaccharide on to the peptide.

For reasons set forth above, one skilled in the art cannot have a reasonable expectation of success to arrive at the present invention by combining the teachings of Meinojohanns, Komba, and Ratcliffe. Therefore, a combination of these references cannot render the amended claim 1 obvious, and the amended claim is patentable over Meinojohanns,

Komba, and Ratcliffe. Dependent claims 5-7 and 22-25 should also be patentable for at least the same reasons. Accordingly, withdrawal of this rejection is respectfully requested.

Conclusion

Applicant believes this reply is fully responsive to all outstanding issues and places this application in condition for allowance. If this belief is incorrect, or other issues arise, the Examiner is encouraged to contact the undersigned or his associates at the telephone number listed below. Please apply any charges not covered, or any credits, to Deposit Account 50-0591, Reference 17563/003001.

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Respectfully submitted,

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